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LETTER TO THE EDITORS

Everolimus-induced recurrent pericardial effusion after kidney transplantation

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Sirs,

After kidney transplantation, adverse effects from mammalian-target of rapamycin inhibitors (mTORi) are frequent, and some are unrecognized [1,2]. Recently, Bertrand *et al.* reported two first cases of sirolimus-induced pericardial effusion after kidney transplantation [3]. Herein, we report a first case of everolimus-induced recurrent pericardial effusion in this setting.

A 60-year-old man received a kidney allograft for chronic tubular-interstitial nephropathy in 1998. Maintenance immunosuppression was based on mycophenolate mofetil (MMF), steroids, and cyclosporine A, which was replaced by everolimus in 2002 because of impaired kidney function. Eight years later, he was admitted for cough, fever (38.8 °C), dyspnea, and hypoxemia. A physical examination revealed bilateral crackles on the base of both lungs and jugular venous distention.

Laboratory tests showed microcytic anemia (hemoglobin level: 8.2 g/dl), C-reactive protein (CRP) at 330 mg/l, a drop in the MDRD-estimated glomerular-filtration rate (eGFR; from 60–17 ml/min), an everolimus trough level of 3.2 ng/ml, proteinuria at 0.5 g/l, and no leucopenia. Urine and blood cultures; serologies for aspergillosis, mycoplasma, and chlamydia; tests for legionella and *Pneumococcus* antigenuria; serum polymerase chain-reaction for cytomegalovirus (CMV); BK virus and Epstein–Barr virus (EBV); as well as direct examination (mycobacteria, *Pneumocystis jiroveci*, *Aspergillus* and yeast) and culture of bronchoalveolar lavage were all negative.

A chest CT-scan showed bilateral-interstitial infiltrates and abundant noncompressive pericardial effusion (20 mm), which was also seen by transthoracic echocardiography (TTE). The left ventricular-ejection fraction was evaluated at 70%. Despite imipenem and linezolid therapies, he developed respiratory failure that required mechanical ventilation. Everolimus and MMF were temporarily stopped. His status then rapidly improved. He was extubated (day 5) and discharged after completing 15 days of IV antibiotics. At discharge, eGFR had returned to baseline values, CRP had decreased to 18 ng/ml, and everolimus and MMF were re-initiated.

Three months later, a TTE revealed an unchanged abundant circumferential pericardial effusion (20 mm), without compression of the right cavities. Diuretic dosage was increased. One month later, he was re-admitted for right heart failure. A TTE showed a compressive tamponade that required a pericardiocenthesis, and a catheter was maintained in place for 2 days. An exudative (protein level at 40 g/l) lemon-colored fluid (500 ml) was retrieved. The above work-up was redone and was still negative. Pericardial fluid and cultures were negative for bacteria, CMV, EBV, and mycobacteria. TTE, performed 48 h after removal of the pericardial catheter, showed minimal residual effusion. Thereafter, the size of the pericardial effusion increased progressively: 2 weeks later, it was circumferential but noncompressive. Because no infectious or malignant cause was found, it was attributed to everolimus, which was then replaced by tacrolimus. TTE then showed regression of the effusion, which had disappeared by 3 months later. No relapse has been observed thereafter.

The clinical presentation and the late-onset of pericardial effusion under everolimus were very similar to that reported in kidney-transplant patients treated with sirolimus. Hence, pericardial effusion can be considered as a side-effect of mTORi, which should be stopped if there is pericardial effusion without any identified cause.

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